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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/070,297 | 03/05/2002 | Bruno Tocque | 50146/002002 | 2833 |

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|---|---|
| SISSON, BRADLEY L | |
| ART UNIT | PAPER NUMBER |
| 1634 | |

DATE MAILED: 07/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/070,297 | TOCQUE ET AL. | |
| | Examiner | Art Unit | |
| | Bradley L. Sisson | 1634 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *19 May 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *27,29-33,44 and 47-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27,29-33,44 and 47-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *03/05/2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Specification*

1. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

2. Acknowledgement is made of the amendment to said title in the response of 19 May 2006. Said amended title refers to "methods and compositions," however, none of the claims are drawn to any compositions. (Emphasis added)

3. The amendment filed 19 May 2006 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material, which is not supported by the original disclosure, is as follows: The insertion of a phrase into the specification at numerous locations that various documents have now been "incorporated by reference." The fact that the specification, as originally filed, did not specifically state that each of these documents was being incorporated by reference, and also indicated for what reason they were being incorporated by reference, does not now lend support to the position that applicant had intended to incorporate these documents. As set forth in the reproduced section of MPEP 608.01(p)(I)(A)(2), "This correction cannot be made when the material was merely referred to and there was no clear specific intent to incorporate it by reference."

4. Applicant is required to cancel the new matter in the reply to this Office Action.

***Double Patenting***

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

6. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

7. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 27, 29-33, 44 and 47-49 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 6,372,432 B1 (Tocque et al.). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to methods of detection of pathological conditions.

*a.* *Response to argument*

9. Acknowledgement is made of where at pages 18 of the response of 19 May 2006, hereinafter the response, applicant's representative agrees to provide a terminal disclaimer "once otherwise allowable subject matter has been determined."

***Claim Rejections - 35 USC § 112***

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 27, 29-33, 44, and 47-49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Attention is directed to the decision in *University of Rochester v. G.D. Searle & Co.* 68 USPQ2D 1424 (Fed. Cir. 2004) at 1428:

> To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. Vas-Cath, 935 F.3d at 1563; see also Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572 [41 USPQ2d 1961] (Fed. Cir. 1997) (patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention"); In re Gosteli, 872 F.2d 1008, 1012 [10 USPQ2d 1614] (Fed. Cir. 1989) ("the description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed"). Thus, an applicant complies with the written-description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572.

For convenience, claim 27 is reproduced below.

27. (Currently Amended) A method for the remote detection *in vitro* of the presence of a given, predefined pathological condition associated with a deregulation in a cell signaling pathway in a human subject, wherein said method comprises ~~comprising~~:

(i) providing a sample of blood cells from the subject, wherein said blood cells comprise lymphocytes, macrophages, monocytes or dendritic cells,

(ii) preparing nucleic acid molecules from the sample, and

(iii) obtaining a hybridization profile by hybridizing all or part of the nucleic acid molecules so prepared with at least one nucleic acid library comprising a plurality of nucleic acid molecules specific for differentially spliced ribonucleic acid molecules (RNAs) expressed in blood cells from human subjects having the given, predefined pathological condition, wherein

(a) expression of the differentially spliced RNAs is characteristic of the given, predefined pathological condition, ~~and wherein~~

(b) said blood cells from human subjects having the given, predefined pathological condition comprise lymphocytes, macrophages, monocytes, or dendritic cells, and wherein

(c) the pathological condition affects a tissue distinct from said blood cells,

wherein the hybridization profile indicates ~~indicating~~ the presence of said given, predefined pathological condition in said subject.

11. Claim 27 has been amended and claims 47-49 have been added. At page 15 of the response received 19 May 2006, applicant's representative asserts that support for the new limitations can be found at page 2, lines 27-30, and at page 3, lines 9-11. A review of the cited passages fails to find support for the new claims and for the new limitations inserted into claim

27. Accordingly, and in the absence of convincing evidence to the contrary, the newly added material constitutes new matter.

12. A review of the specification fails to find where applicant had contemplated, much less fully described, pathologies other than cancer, stenosis and neurodegenerative disorders as being applicable to a general method of detecting pathologies in organisms, much less to detecting such pathologies in humans and then using only lymphocytes, macrophages, monocytes or dendritic cells, to which clam 27is now limited. Indeed, the specification has not identified any specific form of cancer that can be identified from these cells, much less teach what an informative hybridization profile would look like.

13. While an applicant is not required to provide examples of their invention, it is noted that the only part directed to diagnosis of pathologies in humans is that found at pages 28-30, and then the disclosure is found to contain numerous instances of employing forward-looking statements a to what is "possible" and/or "very probable." Neither pages 28-30 nor any other part of the disclosure has been found to set forth a full, clear, and concise description of the invention such that one would be able to identify any human cancer, much less cancers such as solid tumors of the liver, lungs, head and neck, melanoma, liver, bladder, breast, etc., or for that matter, any other human pathology.

14. Absent the requisite description, and having found in its absence numerous instances of forward-looking statements, the specification does not reasonably suggest that applicant was in possession of the invention at the time of filing.

15. Therefore, and in the absence of convincing evidence to the contrary, claims 27, 29-33, 44, and 47-49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

*Response to argument*

16. At page 20, bridging to page 23 of the response received19 May 2006, hereinafter the response, applicant's representative quotes from *Hybritech Incorporated v. Monoclonal Antibodies, Inc.* 231 USPQ 81, 93 "The written description standard **does not require** a detailed description of those features of an invention that were well known to or understood by the skilled artisan at the time of filing, but rather, '[t]he description need only describe in detail that which is new or not conventional.'

17. The above argument has been fully considered and has not been found persuasive as the issue at hand in *Hybritech* from which the cited passage was lifted dealt not with satisfaction of the written description requirement, but rather, with the satisfaction of the enablement requirement. Accordingly, the decision in *Hybritech* is nonanalogous to that of the instant application. Attention is directed to the decision of *Vas-Cath Inc. v. Mahurkar* 19 USPQ2d 1111 (CAFC, 1991):

> This court in *Wilder* (and the CCPA before it) clearly recognized, and we hereby reaffirm, that 35 USC 112, first paragraph, requires a "written description of the invention" which is separate and distinct from the enablement requirement. The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the "applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed.*

18. For the above reasons, and in the absence of convincing evidence to the contrary, the rejection is maintained against previously rejected claims and applied against newly added claims 47-49.

**19.** Claims 27, 29-33, 44, and 47-49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. As set forth in *Enzo Biochem Inc., v. Calgene, Inc.* (CAFC, 1999) 52 USPQ2d at 1135, bridging to 1136:

> To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.' " *Genentech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997) (quoting *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)). Whether claims are sufficiently enabled by a disclosure in a specification is determined as of the date that the patent application was first filed, see *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986).... We have held that a patent specification complies with the statute even if a "reasonable" amount of routine experimentation is required in order to practice a claimed invention, but that such experimentation must not be "undue." See, *e.g.*, *Wands*, 858 F.2d at 736-37, 8 USPQ2d at 1404 ("Enablement is not precluded by the necessity for some experimentation . . . However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' ") (footnotes, citations, and internal quotation marks omitted). In *In re Wands*, we set forth a number of factors which a court may consider in determining whether a disclosure would require undue experimentation. These factors were set forth as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *Id.* at 737, 8 USPQ2d at 1404. We have also noted that all of the factors need not be reviewed when determining whether a disclosure is enabling. See *Amgen, Inc. v. Chugai Pharm. Co., Ltd.*, 927 F.2d 1200, 1213, 18 USPQ2d 1016, 1027 (Fed. Cir. 1991) (noting that the *Wands* factors "are illustrative, not mandatory. What is relevant depends on the facts.").

20. The claimed method is directed to, and encompasses the "remote detection *in vitro*" of any "predefined pathological condition associated with a deregulation in a cell signaling pathway in a human subject."

21. A review of the specification fails to find where any hybridization profile has been determined for any known human pathological condition, much less one associated with a deregulation of a cell signaling pathway.

22. While one is not required to teach each and every possible embodiment encompassed by the claims, the specification has not been found to teach a reproducible method whereby any specific human pathological condition could be identified. In short, applicant has not provided the essential starting materials and reaction conditions needed to practice even a part of the claims' scope. The situation at hand is analogous to that in *Genentech v. Novo Nordisk A/S* 42 USPQ2d 1001. As set forth in the decision of the Court:

> " '[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation.' *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *see also Amgen Inc. v. Chugai Pharms. Co.*, 927 F. 2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed Cir. 1991); *In re Fisher*, 427 F. 2d 833, 166 USPQ 18, 24 (CCPA 1970) ('[T]he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.').
>
> *****
>
> "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. *See Brenner v. Manson*, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (starting, in context of the utility requirement, that 'a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.') Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor,

> or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. "It is true . . . that a specification need not disclose what is well known in the art. *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material or any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skill in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research. (Emphasis added)

23. Furthermore, and as set forth above, the specification does not reasonably suggest that applicant was in possession of the claimed invention at the time of filing. Given that one cannot enable that which they do not yet possess, the instant claims are not enabled by the original disclosure.

24. While the specification has been amended so to recite that various documents are now incorporated by reference, the specification is silent as to how these prior art methods are to be adapted so to yield the now claimed invention.

25. Therefore, and in the absence of convincing evidence to the contrary, claims 27, 29-33, 44, and 47-49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

*Response to argument*

At pages 24-26 argument is presented that the specification is fully enabled, citing passages from the specification, e.g., page 6, line 26 to page 7, line 5; and page 12, line 15, to page 21, line 28.

The above-identified passages have been review and have not been found to set forth in such full, clear, exact, and concise language how the claimed invention is to be practiced. At best, the cited passages provide an invitation for others to experiment. Such generalized statements do not, however, constitute an enabling disclosure.

26. The declaration under 37 CFR 1.132 filed 19 may 2006 is insufficient to overcome the rejection of claims 27, 29-33, 44, and 47-49 based upon 35 USC 112, first paragraph, as set forth in the last Office action because: The level of disclosure found within the declaration is not commensurate with the teachings provided in the specification. It is further noted that declarant is a co-inventor and statements attributed to same do not represent the opinion of a disinterested third party.

27. For the above reasons, and in the absence of convincing evidence to the contrary, the rejection is maintained.

28. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

29. Claims 27, 29-33, 44, and 47-49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

30. Claims 27, 48, and 49 are indefinite with respect to what constitutes the metes and bounds of "remote detection." Claims 29-33 and 44, which depend from claim 27, fail to overcome this issue and are similarly rejected.

***Conclusion***

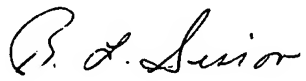
31. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

32. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

33. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571) 272-0751. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

34. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

35. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Bradley L. Sisson
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BLS